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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/693,754	10/20/2000	Neil Berinstein	13115	7885

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
11/17/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/693,754	BERINSTEIN ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-19,21-27 and 32-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-19,21-27 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/23/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/22/09 has been entered. Applicant's amendment and response submitted with the RCE have also been entered. Claims 3, 20, and 28-31 are canceled and new claims 34-35 have been added. Claims 1-2, 4-19, 21-27, and 32-35 are pending in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in the instant action can be found in the previous office action.

Claim Rejections - 35 USC 103

The rejection of claims 1-2, 4-17, and 32-33 under 35 U.S.C. 103(a) as being unpatentable over Hurpin et al. (1998) Vaccine, Vol. 16 (2/3) 208-215, in view of Hodge et al. (1997) Vaccine, Vol. 15, No. 6/7, 759-768, US Patent No. 6,127,116 (10/3/00), filed on 3/4/97 and hereafter referred to as Rice et al., and Lehner et al. (1999) J. Infect. Dis., Vol. 179 (Suppl 3), S489-S492, is maintained over previously pending and new claims 1-2, 4-17, and 32-35.

Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant provides arguments against each reference individually but states that they understand that the rejection is based on the combined teachings of Hurpin et al., Hodge et al., Rice et al. and Lehner et al.

The applicant argues that the examiner has misrepresented the teachings of Hurpin et al. by stating that Hurpin et al. teaches lymphatic administration to spleen or lymph node, when in fact Hurpin et al. only teaches intrasplenic administration and does not mention lymphatic tissue. In response, it is first noted that the applicant's representative has misquoted the examiner. The bottom paragraph of page 7 of the response states:

> The examiner's allegation that Hurpin teaches delivery "to lymphatic tissue, whether spleen or lymph node" is an incorrect characterization of what the reference actually discloses.

The examiner did not in fact make this "allegation". The entire sentence from the previous office action reads, " [t]hus, based on the teachings of Hurpin et al., the skilled artisan would have expected that delivery of vaccine to lymphatic tissue, whether spleen or lymph node, would generate increased immune responses over subcutaneous delivery". From the text of the full sentence it is clear that the examiner has not stated that Hurpin teaches administration to spleen or lymph node, the examiner states that the skilled artisan having read Hurpin et al. would have expected that delivery of a vaccine to a lymphatic tissue, whether splenic or lymph node, would be capable of generating an increased immune response over subcutaneous delivery. Thus, the examiner has not misinterpreted or mischaracterized Hurpin et al. Further, there is no dispute that Hurpin et al. teaches intrasplenic delivery. There is also no dispute that the spleen is a lymphatic

tissue. Thus, by teaching administration to the spleen, Hurpin et al. clearly teaches delivery to a lymphatic tissue.

The applicant then reiterates their argument that the technique used by Lehner et al. is similar to applicant's control subcutaneous injection technique because in their opinion a subcutaneous administration is "just under the skin" and therefore Lehner et al. delivered their antigen 2-4 cm from the iliac lymph node. According to their argument, the control technique disclosed in the specification administered antigen subcutaneously in the dorsal cervical/interscapular region, a region which comprises many lymph nodes, such that this technique is similar to Lehner's. In response, Lehner et al. was cited for demonstrating that the delivery of an antigen such that the lymph node is specifically targeted generates increased immune responses to the antigen as compared to other routes of administration. As stated in previous office actions, Lehner et al. showed that a direct comparison of intramuscular versus intradermal versus targeted iliac lymph node immunization revealed that targeted iliac lymph node administration of antigen resulted in increased T and B cell mediated antigen-specific immune responses (Lehner et al., page S489, and page S491). The targeted iliac lymph node administration technique, while subcutaneous, administers the antigen close to both the internal and external iliac lymph nodes, ensuring direct exposure of the lymph nodes to the administered antigen. Applicant's argument that the Lehner method results in delivery of the antigen about 2-4 cm from the closest lymph node and that somehow this makes the targeted iliac lymph node immunization technique of Lehner analogous to applicant's non-targeted subcutaneous injection has not been found persuasive. Applicant's arguments regarding the Lehner et al. technique are based on an earlier paper, Lehner et al. (1994) J. Immunol., Vol. 153, 1858-1868. However, as

discussed in the previous office action, the cited passage from the 1994 paper teaches that the internal iliac lymph node is found distal to the femoral vessels and about 2 to 4 cm s.c. This passage does not state that the targeted delivery technique of Lehner delivers the vaccine 2-4 cm from a lymph node. This passage states that the iliac lymph nodes are located 2-4 cm subq and just distal to the femoral vessels. Further, subcutaneous is defined as meaning below the skin, see for example the Merriam-Webster Online Dictionary definition for "subcutaneous". The use of the term "subcutaneous" administration does not place any specific distance limitation on the injection. In addition, the 1994 paper cited by applicant provides evidence that the location of the internal iliac lymph node was known at the time of filing such that a subcutaneous injection could be directed close to the internal iliac lymph node. In contrast, applicant's subcutaneous administration technique was not designed to target any particular lymph nodes, and there is no indication in the specification that the applicant's subcutaneous injections were in fact administered in close proximity to any particular lymph node or nodes in the dorsal cervical/ interscapular regions. In addition, the fact that the Lehner et al. publication cited in the instant rejection generated substantial antigen specific immune responses using their targeted iliac lymph node immunization technique whereas both Hurpin et al. and applicant's were not able to generate antigen specific immune responses greater than controls using non-targeted subcutaneous administration provides clear evidence that targeted delivery of antigen in the vicinity of lymph node has a substantial effect in enhancing immune responses. Thus, applicant's subcutaneous administration technique resembles that of Hurpin et al. and is not analogous to the targeted lymph node administration technique used successfully by Lehner et al.

The applicant also reiterates their argument that Rice et al. does not provide sufficient support for an obviousness rejection and further cites *PharmaStem Therapeutics Inc. v. Viacell Inc.* for the need for more than simply general guidance to establish obviousness. In response, the previous office action pointed out that Rice et al. specifically teaches that administration both directly and indirectly to a lymph node is the preferred method of immunization. Thus, Rice et al. provides clear direction to preferentially use direct intranodal administration to induce immune responses. As for *PharmaStem Therapeutics Inc. v. Viacell Inc.,* the portion cited by the applicant's is actually a discussion of how *In re O'Farrell* provided guidance in the *PharmaStem* case. However, as in *PharmaStem*, the instant rejection is not one in which the prior art gave no direction as to which parameters were critical or as to which of many possible routes of choices would be likely to be successful, nor is the instant rejection one in which only general guidance was provided by the cited prior art. In the instant case, all of the cited references teach the importance of the route of administration of antigen on generating immune responses. Further, Hurpin et al. specifically teaches administration to spleen, a lymphatic tissue, and Lehner et al. and Rice et al. specifically teach either the indirect or direct targeting of antigen to a lymph node. Therefore, applicant's arguments are not found persuasive and the rejection of record stands.

The rejection of claims 18-19 under 35 U.S.C. 103(a) as being unpatentable over Hurpin et al. (1998) Vaccine, Vol. 16 (2/3) 208-215, in view of Hodge et al. (1997) Vaccine, Vol. 15, No. 6/7, 759-768, US Patent No. 6,127,116 (10/3/00), filed on 3/4/97 and hereafter referred to as Rice et al., and Lehner et al. (1999) J. Infect. Dis., Vol. 179 (Suppl 3), S489-S492, as applied to claims 1-2, 4-17, and 32-35 above, and further in view of Zaremba et al. (1997) Canc. Res., Vol.

57, 4570-4577 and Salgaller et al. (1996) Canc. Res., Vol. 56, 4749-4757, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

Applicant's arguments are based on their previous argument that Hurpin in view of Hodge, Rice, and Lehner do not support a *prima facie* case of obviousness. These arguments have been fully considered and addressed in detail above and have not been found persuasive. Applicant's further argument that Zaremba et al. and Salgaller et al. do not overcome the deficiencies of Hurpin, Hodge, Rice, and Lehner is not persuasive as the teachings of Hurpin, Hodge, Rice, and Lehner stand, as discussed above, and Zaremba and Salgaller were not cited to teach lymph node administration, rather these references were cited to provide teachings and motivation to immunize with tumor antigens which comprise the sequence YLSGADLNL or YLEPGPVTV. The applicant has not traversed these teachings, therefore, the rejection of record stands.

The rejection of claims 21-27 under 35 U.S.C. 103(a) as being unpatentable over Hurpin et al. (1998) Vaccine, Vol. 16 (2/3) 208-215, in view of Hodge et al. (1997) Vaccine, Vol. 15, No. 6/7, 759-768, US Patent No. 6,127,116 (10/3/00), filed on 3/4/97 and hereafter referred to as Rice et al., and Lehner et al. (1999) J. Infect. Dis., Vol. 179 (Suppl 3), S489-S492, as applied to claims 1-2, 4-17, and 32-35 above, and further in view of Barnett et al. (1997) Vaccine, Vol. 15(8), 869-873, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

Applicant's arguments are based on their previous argument that Hurpin in view of Hodge, Rice, and Lehner do not a *prima facie* case of obviousness These arguments have been fully considered and addressed in detail above and have not been found persuasive. Applicant's further argument that Barnett does not overcome the deficiencies of Hurpin, Hodge, Rice, and Lehner is not persuasive as the teachings of Hurpin, Hodge, Rice, and Lehner stand and Barnett was not cited to teach lymph node administration, rather Barnett was cited to provide teachings and motivation to immunize using a prime/boost vaccination strategy which includes a priming step with a nucleic acid encoding an antigen and a boosting step with a protein form of the antigen. The applicant has not traversed these teachings, therefore, the rejection of record stands.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the

USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633